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Effects of 77 Chemicals on Reproduction in Male and Female Coturnix Quail

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Seventy-one chemicals were administered as single oral doses at about 50% of the estimated LD_{50} to adult male Coturnix quail (*Coturnix coturnix*). None reduced the fertility of eggs produced by female mates by more than 50%. Of six additional chemicals similarly administered to female quail at 24 to 56% of the estimated LD_{50}, only one, *P,P*-bis(1-aziridinyl)-*N*-phenylphosphinic amide, reduced expected egg fertility by more than 50%.

INTRODUCTION

The Denver Wildlife Research Center maintained an avian-chemosterilant screening program from 1972 to 1978, using Coturnix quail (*Coturnix coturnix*) to search for chemicals that affect reproduction in male birds (Schafer *et al.*, 1977). This program and associated field studies were designed to define the biological and ecological aspects of red-winged blackbird (*Agelaius phoeniceus*) reproduction (Bray *et al.*, 1975) and to find safe and effective single-dose avian male chemosterilants that could be used to reduce bird populations and thus damage in agricultural and urban areas. In our earlier laboratory evaluations of 51 chemicals as potential avian chemosterilants (Schafer *et al.*, 1976, 1977), 8 were determined to temporarily or permanently sterilize male Coturnix quail. All of the chemicals tested in these two papers were selected because the literature indicated that these compounds might affect reproduction in birds. In this paper we are presenting the results of our quail reproductive tests with an additional 71 chemicals that were selected from commercial sources, some of which were structurally related to one or more of the compounds tested previously. We have also included data on the gross reproductive effects of six male chemosterilants identified in Schafer *et al.* (1976) on the egg fertility of females treated with single doses of the candidate chemical.

MATERIALS AND METHODS

Details of the methodology we used in testing quail have been published (Schafer *et al.*, 1976, 1977). In summary, the method involves gavaging groups of seven fertile male quail once with about 50% of the estimated LD_{50} dose of the candidate chemical and observing the egg fertility of their female mates for six or seven 5-day periods. At the end of this 30- to 35-day period, the males were sacrificed and

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TABLE 1

FERTILITY OF EGGS PRODUCED BY FEMALE QUAIL AFTER THEIR MATES WERE GIVEN A SINGLE ORAL DOSE OF A CHEMICAL

Chemical	CAS registry number	Male[a] Coturnix LD_{50} (mg/kg)	Male treatment (mg/kg)	Fertility (% of eggs laid that were fertile)		Male mortality	Testes weight (g)
				Days 1–35	Days 20–35		
1. Control (1,2-propanediol)	57-55-6	>2080	2080	92	91	0	2.854
2. Acetamide, 2-(dimethylamino)-*N,N*-dimethyl-	13574-14-6	>316	316	81	78	0	4.453
3. Acridinium, 3,6-diamino-10-methyl-, chloride	86-40-8	>100	100	77[b]	67[b]	0	3.636
4. Ajmalan-17,21-diol, (17*R*, 21α)-	4360-12-7	<316	100	82	81	0	3.420
5. Aziridine, 1-(2-methyl-1-oxopropyl)-	20286-12-8	>316	316	70	60	0	3.107
6. Aziridine, 1-(1-naphthaleneylcarbonyl)-	23383-23-5	>316	316	91	88	0	4.052
7. 1-Aziridinepropanenitrile	1072-66-8	5.62	3.16	85	82	0	3.662
8. Aziridino(2′, 3′:3,4)pyrrolo (1,2*a*) indole-4,7-dione, 6-amino-8(((aminocarbonyl)oxy)-methyl)-1,1*a*,2,8,8*a*,8*b*-hexahydro-8*a*-methoxy-5-methyl-	50-07-7	>100 ♀	10	75	65	0	3.150
9. Bacitracin	1405-87-4	>316	316	86[b]	82[b]	0	3.464
10. 1,2-Benzenediamine, *N,N,N,N*-tetramethyl-	701-01-8	>316	316	93	98	0 (5)[c]	3.352
11. 1,4-Benzenediamine, *N,N,N′,N′*-tetramethyl-	100-22-1	42.1	31.6	89	98	4	3.032
12. Benzenesulfonic acid, 4-methyl-	104-15-4	>316	316	83	83	0	3.667

13. Benzenesulfonic acid, 4,4'-(3-(2-pyridinyl)-1,2,4-triazine-5,6-diyl) bis-, disodium salt	28048-33-1	>316	316	84	81	0	3.515
14. Benzenesulfonic acid, 2,4,6-trinitro-	2508-19-2	>316	316	86	81	0	3.790
15. Benzoic acid, 4-amino-3-butoxy-2-(diethylamino)ethyl ester	99-43-4	100	100	83	87	3	3.094
16. Bicyclo(2.2.1)heptane-1-methanesulfonic acid, 7,7-dimethyl-2-oxo-	762-66-2	>316	316	85[b]	81[b]	0	3.000
17. (1,1'-Biphenyl)-4,4'-diamine, 3,3',5,5'-tetramethyl-	54827-17-7	>316	316	89	88	0	4.193
18. 4,4'-Bipiperidine, 1,1'-bis(2-chloroethyl)-	6802-93-3	75.0	56.2	68	82	0	3.970
19. 1,4-Butanediamine, *N,N,N',N'*-tetramethyl-	111-51-3	>316	316	91	98	1 (5)	4.119
20. 2-Butyne-1,4-diamine, *N,N,N',N'*-tetramethyl-	111-53-5	>316	100	88	89	0	3.709
21. 2-Butyne-1,4-diol	110-65-6	75.0 ♀	56.2	75	80	1	3.346
22. Cinchonan-9-ol, (8α, 9*R*)	485-71-2	>316	316	66[b]	52[b]	0	3.380
23. Cyclopentanecarboxylic acid, 1-amino-	52-52-8	>316	316	85[b]	78[b]	0	3.679
24. 1,2-Ethanediamine, *N,N'*-bis(2-(dimethylamino)ethyl)-*N,N'*-dimethyl-	3083-10-1	>316	316	83	84	0	3.511
25. 1,2-Ethanediamine, *N,N,N',N'*-tetramethyl-	110-18-9	>316	316	89	94	0	3.984
26. Ethanedithioamide, *N,N'*-dimethyl-	120-79-6	17.8 ♂ & ♀	10.0	71	75	0	3.250
27. Ethanesulfonic acid, 2-(bis(2-hydroxyethyl) amino)-	10191-18-1	>316	316	93	94	0	4.465

TABLE 1—*Continued*

Chemical	CAS registry number	Male[a] Coturnix LD_{50} (mg/kg)	Male treatment (mg/kg)	Fertility (% of eggs laid that were fertile)		Male mortality	Testes weight (g)
				Days 1–35	Days 20–35		
28. *D*-glucose, 5-thio-	20408-97-3	>316	316	86	91	0	4.432
29. Guanidine, *N*-butyl-*N'*-nitro-*N*-nitroso-	13010-08-7	>316	316	76[b]	88[b]	0	3.661
			316	88	83	0 (3)	3.451
30. Hydrazinecarbothioamide, *N*-cyclohexyl-	21198-18-5	>316	100	90	85	2	3.193
31. Hydrazinecarboxylic acid, ethyl ester	4114-31-2	100	56.2	87	84	1	3.656
32. Methanediamine, *N,N,N',N'*-tetramethyl-	51-80-9	>316 ♀	316	77	90	3	3.594
33. Methanone, diphenyl, bis(dimethylamino) deriv.	58211-66-8	>316	100	94	89	0	3.211
34. 4-Morpholineethane-sulfonic acid	4432-31-9	>316	316	70	71	1	3.291
35. 4-Morpholinepropane-sulfonic acid	1132-61-2	>316	316	88	87	0	3.753
36. 1-Piperazineethanesulfonic acid, 4-(2-hydroxyethyl)-	7365-45-9	>316	316	65	62	1	3.246
37. 1-Piperazinepropane-sulfonic acid, 4-(2-hydroxyethyl)-	16052-06-5	>316	316	76	73	0	3.819
38. Piperidine, 2-propyl-, (*S*)-	458-88-8	56.2	40	86	80	2	3.399
39. 1,3-Propanediamine, *N,N,N',N'*-tetramethyl-	110-95-2	>316	100	70	73	0	3.764
40. 1-Propanesulfonic acid, 3-(cyclohexylamino)-	1135-40-6	>316	316	90	85	0	3.214
41. 2-Propanol, 1,3-bis(dimethylamino)-	5966-51-8	>316	100	95	96	0	3.802
42. Propiophenone, 4'-amino	70-69-9	>316	316	81	82	0	3.670
43. 1*H*-Purine, 6-chloro-	87-42-3	>316	316	87[b]	78[b]	0	3.627

44. 1*H*-Purine-2,6-dione, 7-(2-chloroethyl)-3,7-dihydro-1,3-dimethyl-	5878-61-5	>100	100	68[b]	76[b]	0	3.574
45. Pyridine, 4-chloro-	626-61-9	>316	316	76[b]	65[b]	0	3.886
46. 3-Pyridinesulfonic acid	636-73-7	>316	316	83	76	0	3.956
47. 1,2,4-Thiadiazol-5-amine, 3-phenyl-	17467-15-1	75.0 ♀	56.2	78	88	0	3.113
48. 1,3,4-Thiadiazol-2-amine, 5-methyl-	108-33-8	>316	316	91	89	1	3.333
49. 1,3,4-Thiadiazole, 2,5-bis(4-piridinyl)-	15311-09-8	>316	316	84	76	0	3.507
50. 1,3,4-Thiadiazolidine-2,5-dithione	1072-71-5	>316	316	84	77	0	3.421
51. 1,2,3,4-Thiatriazol-5-amine, *N*-phenyl-	13078-30-3	>316	316	91	95	0	3.455
52. Thiosulfuric acid, *S*-(2-(dimethylamino) ethyl)ester	14013-30-0	>316	316	90	88	0	3.696
53. 1,2,4-Triazin-3-amine	1120-99-6	>316	316	87	89	1	3.609
54. 1,3,5-Triazin-2-amine, 4-(4-morpholinyl)-	2045-25-2	>316	316	94	93	0 (6)	3.297
55. 1,3,5-Triazine	290-87-9	237 ♀	178	84	85	0	3.988
56. *as*-Triazine, 3-amino-5,6-dimethyl-	17584-12-2	>316	316	87	90	0	3.561
57. 1,3,5-Triazine-4,6-diamine, 2-chloro-	3797-62-4	>316	316	71	76	1 (6)	3.798
58. 1,2,4-Triazine-3,5-(2*H*, 4*H*)-dione	461-89-2	>100	316	92	88	0	3.386
59. 1,2,4-Triazine-3,5-(2*H*, 4*H*)-dione, 2-β-*D*-ribofuranosyl-	54-25-1	>316	316	84[b]	82[b]	0	3.474
60. 1,2,4-Triazine, 5,6-diphenyl-3-(2-pyridinyl)-	1046-56-6	>316	316	91	91	1	4.343
61. 1,3,5-Triazine, 2,4,6-triphenoxy-	1919-48-8	>316	316	95	97	0	3.958

TABLE 1—*Continued*

Chemical	CAS registry number	Male[a] Coturnix LD_{50} (mg/kg)	Male treatment (mg/kg)	Fertility (% of eggs laid that were fertile)		Male mortality	Testes weight (g)
				Days 1–35	Days 20–35		
62. 1,3,5-Triazine, 2,4,6-tri-2-pyridinyl-	3682-35-7	>316	316	85	73	0	3.771
63. 1,3,5-Triazin-2(1*H*)-one, 4-amino-	931-86-2	>316	316	72[b]	72[b]	0	3.464
64. 1,3,5-Triazin-2(1*H*)-one, 4-amino-1-*β*-*D*-ribofuranosyl-	320-67-2	>100	56.2	72	73	0 (6)	2.994
65. 1*H*-1,2,4-Triazol-3-amine	61-82-5	>316	316	81	94	2	3.694
66. 4*H*-1,2,4-Triazol-4-amine	584-13-4	>316	316	87	93	0	3.685
67. 1*H*-1,2,4-Triazole	288-88-0	>316	316	86	79	0	3.746
68. 1*H*,1,2,4-Triazole-3,5-diamine	1455-77-2	>316	316	87	89	0	3.794
69. 3*H*,1,2,4-Triazole-3-thione, 5-amino-1,2-dihydro-	16691-43-3	>316	316	82	83	0	3.382
70. Tricyclo(3.3.1.1^{3,7})-decan-1-amine	768-94-5	>316	316	88[b]	96[b]	0	3.836
71. Urea, tricyclo (3.3.1.1^{3,7})dec-1-yl-	13072-69-0	>316	316	61[b]	50[b]	0 (6)	3.299
72. Uridine, 5-bromo-2'-deoxy-	59-14-3	>100	316	70	67	0	4.011

[a] Unless otherwise noted.
[b] Tests run for 30 days only.
[c] Numbers in parentheses indicate total number of quail pairs used in test if less than seven.

TABLE 2

FERTILITY OF EGGS PRODUCED BY FEMALE QUAIL AFTER THEY WERE GIVEN ORAL DOSES OF SIX CHEMOSTERILANTS

Chemical	CAS registry number	Female Coturnix LD_{50} (mg/kg)	Female treatment (mg/kg)	Fertility (% of eggs laid that were fertile)		Female mortality[a]
				Days 1–35	Days 20–35	
1. Control (1,2-propanediol)	57-55-6	>2080	2080	90	89	0
73. Aziridine,1,1′,1″-phosphinothioylidynetris-	52-24-4	237	133	64	85	0
74. *P,P*-Bis(1-aziridinyl)-*N*-cyclohexylphosphinothioic amide	3054-21-5	>316	100	58	69	0 (6)
75. *P,P*-Bis(1-aziridinyl)-*N,N*-dimethylphosphinothioic amide	3750-43-4	75.0	31.6	83	90	0
76. *P,P*-Bis(1-aziridinyl)-*N*-phenylphosphinic amide	6784-53-8	237	56.2	42	40	4
77. *P,P*-Bis(1-aziridinyl)-*N*-phenylphosphinothioic amide	25033-34-5	>316	316	55	72	1(4)
78. *s*-Triazine, 2,4,6-tris(1-aziridinyl)-	51-18-3	133	31.6	82	86	0

[a] Numbers in parentheses indicate the total number of pairs tested if different from seven.

their testes extracted and weighed. On the basis of previous results, we selected two accept–reject criteria to indicate those chemicals with sufficient chemosterilant activity to warrant additional investigation: a fertility rate of 40% or less for the final 15 days of the test (a 50% reduction from control fertility rates) and a combined testes weight of 1.100 g or less at sacrifice.

We used the same methods for our tests on females, except that we are not reporting the weight of the ovaries or the rest of the female reproductive tract because of large weight variations, depending upon the stage of egg development at sacrifice. The single accept–reject criterion established for females was ≤40% fertility for the final 15 days of the test.

RESULTS AND DISCUSSION

None of the 71 chemicals tested in male quail met our accept–reject criteria (Table 1), indicating that our chemical selection methods were not very effective in obtaining chemicals with sufficient activity to investigate further as avian chemosterilants. Therefore, we have determined that further testing of candidate male avian chemosterilants in our laboratory will be limited only to those chemicals with demonstrated chemosterilant activity in other animal species, such as insects and mammals. The data gathered, however, on the effects of these 71 chemicals on reproduction in male quail should be useful to partially indicate the potential ability of these chemicals to affect avian reproduction when they are encountered as environmental pollutants.

Of the six chemicals tested in females (Table 2), only one, *P,P*-bis(1-aziridinyl)-*N*-phenylphosphinic amide, met our criterion for acceptable activity. This compound is worthy of further investigation in the laboratory and/or field to verify its activity as a potential avian chemosterilant when used for control purposes or when encountered as a pollutant.

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